IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Howard Sinkinson Marsden, Nigel Dennis Stow, and Gordon William McLean	: Art Unit: : Examiner: :
Serial No.:	(to be assigned)	:
Filed:	(herewith)	:
FOR:	ASSAY FOR SCREENING FOR AN ANTI-VIRAL AGENT	:

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

S I R :

Preliminary to examination in the United States Patent and Trademark Office of a new divisional application filed herewith, please make the following amendments in the above-identified application in order to place it in condition for examination.

TITLE OF THE INVENTION:

On page 1, at line 1, please replace the Title of the Invention with the following:

ASSAY FOR SCREENING FOR AN ANTI-VIRAL AGENT

IN THE SPECIFICATION:

Please amend the specification as follows:

On page 1, before line 3, please insert the following paragraph:

The present application is a divisional application of U.S. Serial No. 09/230,405, filed on January 25, 1999, which has been allowed, which in turn is the U.S. national phase application of PCT International Application No. PCT/GB97/02025 filed 28 July 1997.

Please replace the first paragraph of the specification starting on page 1, lines 3 through 5, with the following:

The present invention relates to an assay for screening for suitable anti-viral agents, particularly but not exclusively the present invention relates to an assay for screening anti-viral agents effective against herpesviruses.

IN THE CLAIMS:

Please cancel claims 1-14.

Please add the following new claims 15-27:

15. (Newly Added) An in vitro assay to determine the ability of a substance to inhibit the association of UL8 and POL wherein "UL8" is defined as UL8 of HSV-1 or the homologues thereof in other herpesviruses and "POL"

is defined as POL of HSV-1 or the homologues thereof in other herpesviruses, said assay comprising:

i) providing a first viral component consisting of UL8;

ii) providing a second viral component consisting of POL;

iii) exposing said first viral component to said substance followed by addition of the second viral component, or exposing said second viral component to said substance followed by addition of the said first viral component, or exposing the first viral component to said second viral component followed by said substance;

iv) washing to remove any second viral component and/or substance not associated with the first viral component; and

v) detecting the presence, and optionally determining the amount, of associated first and second viral components.

16. (Newly Added) The assay as claimed in Claim 15 wherein UL8 of HSV-1 is the first viral component, and POL of HSV-1 is the second viral component.

17. (Newly Added) The assay as claimed in Claim 15 wherein one of UL102 of HCMV is the first viral component and UL54 of HCMV is the second viral component.

18. (Newly Added) The assay as claimed in Claim 15 wherein one of said first and second viral components is localised on a surface.

19. (Newly Added) The assay as claimed in Claim 15 wherein an antibody is used to detect association of said viral components.

20. (Newly Added) An in vitro assay to determine the ability of a candidate substance to inhibit the association of POL and a substance wherein "POL" is defined as POL of HSV-1 or the homologues thereof in other herpesviruses, said assay comprising:

i) providing a polypeptide selected from the group consisting of at least one of;

a) VFTGVLAGVWGEGGKFVYPFDDKMSFLF A (SEQ ID NO:5);

b) IELVFTGVLAGVWGEGGKFV (SEQ ID NO: 7);

c) DEWVRSLAVDAQHAAKRVASEGLRFFRL NA (SEQ ID NO: 11); and

d) TWLEERDEWVRSLAVDAQHAARRVAS (SEQ ID NO: 12).

i) providing a viral component consisting of POL;

ii) exposing said polypeptide to said substance followed by addition of the viral component, or exposing said viral component to said substance followed by addition of the said polypeptide, or exposing said viral component to said polypeptide followed by said substance;

iii) washing to remove any viral component and/or substance not associated with the polypeptide; and

v) detecting the presence, and optionally determining the amount of associated polypeptide and viral component.

21. (Newly Added) An antiviral agent which prevents or hinders replication of a herpesvirus in vitro by specifically binding to POL or UL8 thus inhibiting the association between UL8 and POL, wherein "UL8" is defined as UL8 of HSV-1 or the homologues thereof in other herpesviruses and "POL" is defined as POL of HSV-1 or homologues thereof in other herpesviruses.

22. (Newly Added) An antiviral agent as claimed in Claim 21 which mimics the C-terminal alpha-helical region or the C-terminal tail of UL8.

23. (Newly Added) An antiviral agent as claimed in Claim 21 which is a peptide having a sequence corresponding to the sequence forming the C-terminal tail or the C-terminal alpha-helical region of UL8.

24. (Newly Added) An antiviral agent as claimed in Claim 21, said agent being a non-peptidal compound which mimics a peptide obtained from the C-terminal tail and/or the alpha-helix portion of the C-terminus of UL8.

25. (Newly Added) An antiviral agent which prevents or hinders replication of a herpesvirus in vitro by specifically binding to POL or UL8, thus inhibiting the association between UL8 and POL, wherein "UL8" is defined as UL8 of HSV-1 or homologues thereof in other herpesvirus and "POL" is defined as POL of HSV-1 or homologues thereof in other herpesvirus; wherein said agent comprises a non-peptidal compound which mimics a peptide having an amino acid sequence selected from the group of sequences consisting of:

a) VFTGVLAGVWGEGGKFVYPFDDKMSFLFA (SEQ ID NO:5);

b) IELVFTGVLAGVWGEGGKFV (SEQ ID NO: 7);

c) DEWVRSLAVDAQHAAKRVASEGLRFFRLNA (SEQ ID NO: 11); and

d) TWLEERDEWVRSLAVDAQHAARRVAS (SEQ ID NO: 12).

26. (Newly Added) A method of preventing replication of a herpesvirus, said method comprising providing an agent able to bind specifically to UL8 or POL thereby inhibiting the association between UL8 and POL in

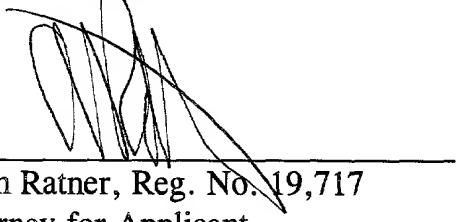
vitro, wherein "UL8" is defined as UL8 of HSV-1 or the homologues thereof in other herpesviruses and "POL" is defined as POL of HSV-1 or the homologues thereof in other herpesvirus, said method comprising adding said agent to said replicating herpesvirus in sufficient quantity to cause said inhibition and monitoring the effect on viral replication and thus determining the presence or extent of said inhibition.

27. (Newly Added) A method of treating a patient for an infection caused by a herpesvirus, said method comprising administering to said patient a therapeutically effect amount of an antiviral agent as claimed in Claim 21.

IN THE ABSTRACT:

Please include an Abstract on a separate sheet as enclosed herewith.

Respectfully submitted,



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The Assistant Commissioner for Patents is hereby authorized to charge payment to Deposit Account No. **18-0350** of any fees associated with this communication.

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Kathleen Libby

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ABSTRACT

An antiviral agent capable of disrupting the association of two viral proteins required for DNA replication in herpesviruses. The agents disrupt the association of UL8 and POL in HSV-1 or the association of equivalent homologues of these proteins in other herpesviruses (for example UL 102 and UL54 in HCMV). Suitable agents are peptides which mimic the C-terminal or C-proximal portion of UL8 (or its homologues) for example the peptide IELVFTGVLAGVWGEGGKFV. Peptidomimetic compounds of such peptides are also suitable anti-viral agents. An assay to test for agents capable of disrupting association of POL and UL8 (or homologues thereof) is also described.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

TITLE OF THE INVENTION:

~~**ANTI-HERPESVIRAL AGENT**~~ **ASSAY FOR SCREENING FOR AN ANTI-VIRAL AGENT**

IN THE SPECIFICATION:

Specification at page 1, prior to line 3:

The present application is a divisional application of U.S. Serial No. 09/230,405, filed on January 25, 1999, which has been allowed, which in turn is the U.S. national phase application of PCT International Application No. PCT/GB97/02025 filed 28 July 1997.

Specification at page 1, lines 3 through 5:

~~The present invention relates to an anti-viral agent effective against herpesviruses and to an assay for screening for other suitable anti-viral agents.~~

The present invention relates to an assay for screening for suitable anti-viral agents, particularly but not exclusively the present invention relates to an assay for screening anti-viral agents effective against herpesviruses.

IN THE CLAIMS:

Claims 1-14 have been cancelled.

Claims 15-27 have been added.